

**REMARKS**

This Amendment is responsive to the Office Action mailed August 25, 2009. With this amendment, all prior pending claims are now canceled, and new claims 9-14 are submitted. Applicants note that the new claims are presented in response to the outstanding Office Action and are intended to address the Action's concerns relating to indefiniteness. In this regard, while Applicants submit that the prior claims were definite, these amendments are made to advance prosecution and are not intended to constitute an acquiescence to or agreement with the Office's rejections under 35 U.S.C. § 112, second paragraph.

Applicants note that the new claims find support throughout the specification, and particularly, for example, in Examples 1-3 (for claims 12-14) and 4 and 5 (for claims 9-11).

Reconsideration and withdrawal of the rejections made in the above-referenced Office Action are respectfully requested in view of the following remarks.

**Claim Rejections 35 U.S.C. § 112, Second Paragraph**

The Office Action rejects all claims pending and under consideration (3-5, 7, and 8) under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office asserts that the claims lack essential steps, such as a) steps for measuring the GPC3 and the means for doing so, and b) steps for comparing the results to a control sample.

In response, Applicants respectfully disagree with the bases of the rejection. Applicants respectfully submit that the lack of a recitation within the claims of the precise means by which GPC3 is measured does not render the scope of the claims indefinite. A person skilled in the art

can easily understand the metes and bounds of the claims. As the caselaw says, "breadth is not indefiniteness."

Applicants also respectfully disagree that recitation of a comparison step to a control value must be included for the claims to be considered definite. Applicants submit that a person skilled in the art would immediately understand the metes and bounds from reading the claims in view of the specification.

Finally, Applicants respectfully submit that the claims need not recite particular values for GPC3 in a test sample in order that a person skilled in the art understand the metes and bounds of the invention.

Nevertheless, despite Applicants' disagreements with the Office about the prior bases for rejection under 35 U.S.C. § 112, second paragraph, Applicants submit herewith amendments that, when considered with all remarks herein, should be responsive to any outstanding issues.

Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Claim Rejections 35 U.S.C. § 112, First Paragraph, Enablement

The Office Action rejects claims 3-5, 7, and 8 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner asserts that the specification enables detecting soluble or membrane associated GPC3 protein using an antibody recognizing an extracellular domain of the protein in a method for diagnosing malignant melanoma along with other

clinically relevant melanoma tumor markers, but does not reasonably provide enablement for the entire claim scope.

Initially, Applicants wish to point out that Applicants have discovered that GPC3 is a marker for malignant melanoma. The Office notes that, in addition to showing that GPC3 expression correlates with the existence of malignant melanoma, the specification shows that GPC3 expression also occurs with pigmented nevi. So that the record is clear, Applicants also wish to point out that (as discussed in the Background Art section of the specification) GPC3 expression has also been correlated with primary hepatocellular carcinoma (HCC). However, Applicants respectfully submit that the fact that GPC3 is also indicative of the presence of other forms of cancer, or of the existence of pigmented nevi, does not discount its value in determining an increased likelihood of the presence of malignant melanoma.

There is quite clearly a great value in knowing that a subject's blood is positive for GPC3, particularly if that subject is believed to be at risk of malignant melanoma. Furthermore, this knowledge certainly is of great diagnostic value, as it may lessen the time needed for the diagnostician to identify a cancerous lesion, or for that diagnostician to conclude that a questionable lesion is malignant melanoma.

Nevertheless, Applicants understand the Office's concerns about whether malignant melanoma can be diagnosed with certainty, given that GPC3 expression also appeared to correlate with the existence of pigmented nevi. Thus, in an attempt to allay any concern in this regard, Applicants have presented amended claims that recite methods for determining an increased likelihood of the presence of malignant melanoma (as opposed to diagnosing malignant melanoma, per se). Applicants respectfully submit that the specification shows that

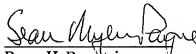
the presence of GPC3 in a subject's sample is indicative of an increased likelihood of the presence of malignant melanoma.

Applicants respectfully submit that the present amendments and remarks are fully responsive to the outstanding rejections under 35 U.S.C. § 112, first paragraph, and respectfully request their withdrawal.

### CONCLUSION

In view of the foregoing remarks and amendments, Applicants respectfully submit that the claims are in condition for allowance. If there should be any questions by telephone, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully Submitted,  
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